

**REMARKS****A. Status of Claims**

Claims 52-82 were pending at the time of the Official Action. No claims have been amended, no new claims have been added, and no claims have been canceled. Therefore, claims 52-82 are currently pending in the case.

**B. The Rejections Under et U.S.C. §102(b) are Overcome****1. Rejections Based on Anderson *et al.* (J. Nuc. Med. 36(5):850-858, 1995)**

Claims 52, 54, 55, 56, 58, 61-67, 69, and 70 have been rejected under 35 U.S.C. §102(b) as being anticipated by Anderson *et al.* (J. Nuc. Med. 36(5):850-858, 1995) ("Anderson *et al.*, (1995)"). According to the Action, Anderson *et al.* (1995) is said to disclose the preparation, biodistribution, and dosimetry of <sup>64</sup>Cu-labeled anti-colorectal carcinoma monoclonal antibody fragments 1A3-F(ab)<sub>2</sub>, wherein the specific species of interest is <sup>64</sup>C-labeled BAT-2-iminothiolate-1A3-Fab'<sub>2</sub>, wherein the linking agent is 2-iminothiolane (2IT). Thus, Anderson *et al.* (1995) is said to disclose a method of imaging a site within a subject that comprises administering a radionuclide-labeled bisaminoethanethiol (BAT) targeting ligand complex and analyzing the radioactive signal by emission tomography. Applicants respectfully traverse.

As an initial matter, it is well-established that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

Anderson *et al.* (1995) fails to anticipate because it does not expressly or inherently disclose any radionuclide-labeled bis-aminoethanethiol targeting ligand conjugate, or detection of a radioactive signal from a site by emission tomography using any such conjugate.

The conjugates set forth in Anderson *et al.* (1995) are not bis-aminoethanethiol targeting ligand conjugates. Anderson *et al.* (1995) defines 6-bromoacetamido-benzyl-1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''tetraacetic acid as "BAT." (see abstract) In contrast, in the present invention, "BAT" refers to a bis-aminoethanethiol chelating ligand. The bis-aminoethanethiol chelating ligands of the instant invention include the availability of two nitrogen atoms and two sulfur atoms for chelation of the radionuclide. In contrast, 6-bromoacetamido-benzyl-1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''tetraacetic acid does not include any sulfur atoms for chelation. Furthermore, including 2-iminothiolane (2IT) as a linker to join the 6-bromoacetamido-benzyl-1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''tetraacetic acid to the 1A3-Fab' fragment does not render the compounds of Anderson *et al.* (1995) bis-aminoethanethiol targeting ligand conjugates. Neither 2IT nor the 6-bromoacetamido-benzyl-1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''tetraacetic acid moiety includes the required ethane backbone structure of a bis-aminoethanethiol or the combination of N and S groups for chelation. Therefore, the <sup>64</sup>Cu-labeled 6-bromoacetamido-benzyl-1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''tetraacetic acid conjugates set forth in Anderson *et al.* (1995) are *structurally distinct* from the radionuclide-labeled bis-aminoethanethiol targeting ligand conjugates of the present invention.

Because Anderson *et al.* (1995) fails to expressly or inherently disclose each limitation of the claimed invention, there can be no anticipation of the claimed invention. Applicants

respectfully request withdrawal of the rejection of claims 52, 54, 55, 56, 58, 61-67, 69, and 70 under 35 U.S.C. §102(b).

**2. Rejections Based on Anderson *et al.* (*J. Nuc. Med.*, 33(9):1685-1691, 1992)**

Claims 52, 53, 55, 56, 58, 61-64, 66, 67, 69, 70, and 79 have been rejected under 35 U.S.C. §102(b) as being anticipated by Anderson *et al.* (*J. Nuc. Med.*, 33(9):1685-1691, 1992) ("Anderson *et al.* (1992)"). The species of interest cited by the Examiner are  $^{64}\text{Cu}$ - or  $^{67}\text{Cu}$ -benzylTETA-1A3 and  $^{64}\text{Cu}$ - or  $^{67}\text{Cu}$ -benzyl-TETA-1A3-F(ab')<sub>2</sub>. According to the Examiner, these species are radionuclide labeled bisaminoethanethiol targeting ligand complexes, since the Anderson *et al.* (1994) purportedly indicates that TETA is another name for BAT. Applicants respectfully traverse.

Anderson *et al.* (1992) fails to anticipate because it does not set forth radiolabeled bis-aminoethanethiol targeting ligand complexes, or any imaging using such complexes. The Examiner is incorrect in her assertion that the species disclosed in Anderson *et al.* (1992) are bisaminoethanethiol targeting ligands. As with the previous rejection, the reference refers to Br-benzyl-TETA as "BAT." See page 1685. However, as discussed above, the TETA species set forth in the reference are not bis-aminoethanethiol chelating ligands. In particular, there are no S atoms available for conjugation in the TETA conjugates. Nor does TETA include the ethane backbone structure of bis-aminoethanethiol conjugates. Thus, TETA is a distinct species from a bisaminoethanethiol chelating ligand. Nor do Applicants find any indication that bis-aminoethanethiol chelating ligands are inherently disclosed in Anderson *et al.* (1992). The reference does not pertain to any radionuclide-labeled bis-aminoethanethiol targeting ligand conjugate.

Because Anderson *et al.* (1992) fails to disclose each and every element of the claimed invention, there can be no anticipation. Therefore, Applicants respectfully request that the rejection of claims 52, 53, 55, 56, 58, 61-64, 66, 67, 69, 70, and 79 under 35 U.S.C. §102(b) should be withdrawn.

**C. The Rejections Under et U.S.C. §103(a) are Overcome**

**1. Rejections of Claims 52, 54, and 57 Based on Anderson *et al.* (1995) in view of Anderson *et al.* (1992)**

Claims 52, 54, and 57 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson *et al.* (1995) in view of Anderson *et al.* (1992). Applicants respectfully traverse.

In rejecting claims under 35 U.S.C. §103, the Examiner bears the initial burden of presenting a *prima facie* case of obviousness. See *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (3) there must be a reasonable expectation of success. *Manual of Patent Examining Procedure* § 2142. See also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991). It is important to note that all three elements must be shown to establish a *prima facie* case of obviousness. Thus, if one element is missing, a *prima facie* case of obviousness does not exist.

There is no *prima facie* case of obviousness because the Examiner has failed to demonstrate that the references teach or suggest any radionuclide-labeled 2-aminoethanethiol

targeting ligand conjugate. The discussion set forth above pertaining to the structures set forth in Anderson *et al.* (1992) and Anderson *et al.* (1995) is herein incorporated into this section.

Furthermore, the Examiner has failed to establish that either Anderson reference teaches or suggest detecting a radioactive signal from a site by emission tomography using a radionuclide-labeled 2-aminoethanethiol targeting ligand conjugate.

Because the Examiner has failed to a teaching or suggestion in the cited references pertaining to each limitation of the claimed invention, he has failed to establish a *prima facie* case of obviousness. Applicants therefore respectfully request that the rejection of claims 52, 54, and 57 under 35 U.S.C. §103(a) based on the combination of Anderson *et al.* (1995) and Anderson *et al.* (1992) should be withdrawn.

## **2. Rejection of Claims 52, 54, and 57 Based on Anderson *et al.* (1995)**

Claims 52, 54, and 57 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson *et al.* (1992).

The Examiner has failed to establish a *prima facie* case of obviousness because he has not met his burden of establishing that Anderson *et al.* (1992) teaches or suggests any radionuclide-labeled 2-aminoethanethiol targeting ligand conjugates. As discussed above, the discussion of which is herein incorporated into this section, the conjugates set forth in Anderson *et al.* are not 2-aminoethanethiol targeting ligand conjugates, but are conjugates that include TETA as the chelator, a species which is structurally distinct from a bis-aminoethanethiol chelating ligand.

Furthermore, the Examiner has failed to establish that Anderson *et al.* (1992) teaches or suggest detecting a radioactive signal from a site by emission tomography using a radionuclide-labeled 2-aminoethanethiol targeting ligand conjugate.

Because the Examiner has failed to set forth any teaching or suggestion in the cited references pertaining to each limitation of the claimed invention, he has failed to establish a *prima facie* case of obviousness. Applicants therefore respectfully request that the rejection of claims 52, 54, and 57 under 35 U.S.C. §103(a) based on Anderson *et al.* (1992) should be withdrawn.

**D. Conclusion**

Applicants believe that the present document is a full and complete response to the Office Action dated June 3, 2005. Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested.

Should the Examiner have any question, please contact the undersigned below at 512-536-5639.

Respectfully submitted,



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